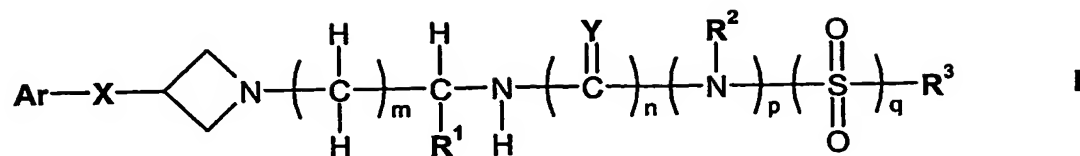


CLAIMS

1. A compound of formula I



in free or salt form, where

Ar is phenyl optionally substituted by one or more substituents selected from halogen,

C₁-C₈-alkyl, cyano or nitro;

R¹ is hydrogen or C₁-C₈-alkyl optionally substituted by hydroxy, C₁-C₈-alkoxy, acyloxy, halogen, carboxy, C₁-C₈-alkoxycarbonyl, -N(R⁴)R⁵, -CON(R⁶)R⁷ or by a monovalent cyclic organic group having 3 to 15 atoms in the ring system;

R² is hydrogen, C₁-C₈-alkyl or C₃-C₁₀-cycloalkyl and R³ is C₁-C₈-alkyl substituted by phenyl, phenoxy, acyloxy or naphthyl, or R³ is C₃-C₁₀-cycloalkyl optionally having a benzo group fused thereto, a heterocyclic group having 5 to 11 ring atoms of which 1 to 4 are hetero atoms, phenyl or naphthyl, said phenyl, phenoxy or naphthyl groups being optionally substituted by one or more substituents selected from halogen, cyano, hydroxy, acyl, nitro, -SO₂NH₂, C₁-C₈-alkyl optionally substituted by C₁-C₈-alkoxy, C₁-C₈-haloalkyl, C₁-C₈-alkoxy, C₁-C₈-haloalkoxy, C₁-C₈-alkylthio, -SO₂-C₁-C₈-alkyl, C₁-C₈-alkoxycarbonyl, C₁-C₈-acylamino optionally substituted on the nitrogen atom by C₁-C₈-alkyl, C₁-C₈-alkylamino, aminocarbonyl, C₁-C₈-alkylamino-carbonyl, di(C₁-C₈-alkyl)amino, di(C₁-C₈-alkyl)aminocarbonyl, di(C₁-C₈-alkyl)aminocarbonyl-methoxy,

or R² and R³ together with the nitrogen atom to which they are attached denote a heterocyclic group having 5 to 10 ring atoms of which 1, 2 or 3 are hetero atoms;

R⁴ and R⁵ are each independently hydrogen or C₁-C₈-alkyl, or R⁴ is hydrogen and R⁵ is hydroxy-C₁-C₈-alkyl, acyl, -SO₂R⁸ or -CON(R⁶)R⁷, or R⁴ and R⁵ together with the nitrogen atom to which they are attached denote a 5- or 6-membered heterocyclic group;

R⁶ and R⁷ are each independently hydrogen or C₁-C₈-alkyl, or R⁶ and R⁷ together with the nitrogen atom to which they are attached denote a 5- or 6-membered heterocyclic group;

R⁸ is C₁-C₈-alkyl, C₁-C₈-haloalkyl, or phenyl optionally substituted by C₁-C₈-alkyl;

X is -C(=O)-, -O-, -CH₂-, or CH(OH);

Y is oxygen or sulfur;

m is 1, 2, 3 or 4; and

n, p and q are each 0 or 1, n+p+q=1 or 2, n+q=1, p+q=1, and when n is 0, p is 0.

2. A compound according to claim 1, in which

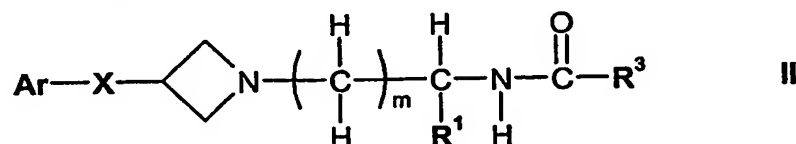
Ar is phenyl substituted by one or two substituents selected from halogen and C₁-C₈-alkyl;
R¹ is hydrogen, C₁-C₄-alkyl optionally substituted by hydroxy or C₁-C₈-alkoxy, acyloxy, C₁-C₈-alkyl substituted by benzoyloxy or phenoxy-C₁-C₄-alkylcarbonyloxy which are optionally substituted in the benzene ring by at least one substituent selected from C₁-C₈-alkoxy, C₁-C₈-alkylcarbonyl and aminosulfonyl, or C₁-C₈-alkyl substituted by naphthyl;
R² is hydrogen or C₁-C₈-alkyl, and R³ is C₁-C₈-alkyl substituted by phenyl or phenoxy, or C₁-C₈-alkyl substituted by benzoyloxy or phenoxy-C₁-C₈-alkylcarbonyloxy which are optionally substituted in the benzene ring by at least one substituent selected from C₁-C₈-alkoxy, C₁-C₈-alkylcarbonyl and aminosulfonyl, or C₁-C₈-alkyl substituted by naphthyl, or R³ is C₃-C₈-cycloalkyl optionally having a benzo group fused thereto, a heterocyclic group having 5 to 11 ring atoms of which one or two are hetero atoms, selected from nitrogen, oxygen or sulfur, or phenyl, benzyl or naphthyl, said phenyl, phenoxy and naphthyl groups being optionally substituted by one, two or three substituents selected from halogen, cyano, nitro, hydroxy, C₁-C₈-alkoxy, C₁-C₈-haloalkoxy, C₁-C₈-alkyl, C₁-C₈-alkylcarbonyl, C₁-C₈-alkylthio, di(C₁-C₈-alkyl)amino or C₁-C₈-alkylcarbonylamino,
or R² and R³, together with the nitrogen atom to which they are attached, denote a heterocyclic group having a N-heterocyclic ring optionally fused to a benzene ring;
X is -O-, -C(=O)- or -CH₂-;
Y is oxygen or sulfur; and
m is 1, 2, 3 or 4.

3. A compound according to claim 1, in which

Ar is phenyl substituted by one or two substituents selected from halogen and C₁-C₄-alkyl;
R¹ is hydrogen, C₁-C₄-alkyl optionally substituted by hydroxy or C₁-C₄-alkoxy, acyloxy, C₁-C₄-alkyl substituted by benzoyloxy or phenoxy-C₁-C₄-alkylcarbonyloxy which are optionally substituted in the benzene ring by at least one substituent selected from C₁-C₄-alkoxy, C₁-C₄-alkylcarbonyl and aminosulfonyl, or C₁-C₄-alkyl substituted by naphthyl;
R² is hydrogen or C₁-C₄-alkyl, and R³ is C₁-C₄-alkyl substituted by phenyl or phenoxy, or C₁-C₄-alkyl substituted by benzoyloxy or phenoxy-C₁-C₄-alkylcarbonyloxy which are optionally substituted in the benzene ring by at least one substituent selected from C₁-C₄-alkoxy, C₁-C₄-alkylcarbonyl and aminosulfonyl, or C₁-C₄-alkyl substituted by naphthyl, or R³ is C₅-C₈-cycloalkyl optionally having a benzo group fused thereto, a heterocyclic group having 5 to 11 ring atoms of which one or two are hetero atoms, selected from nitrogen, oxygen or sulfur, or phenyl, benzyl or naphthyl, said phenyl, phenoxy and naphthyl groups being optionally

substituted by one, two or three substituents selected from halogen, cyano, nitro, hydroxy, C₁-C₄-alkoxy, C₁-C₄-haloalkoxy, C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl, C₁-C₄-alkylthio, di(C₁-C₄-alkyl)amino or C₁-C₄-alkylcarbonylamino,
 or R² and R³, together with the nitrogen atom to which they are attached, denote a heterocyclic group having a N-heterocyclic ring optionally fused to a benzene ring;
 X is -O-, -C(=O)- or -CH₂-;
 Y is oxygen or sulfur; and
 m is 1, 2, 3 or 4.

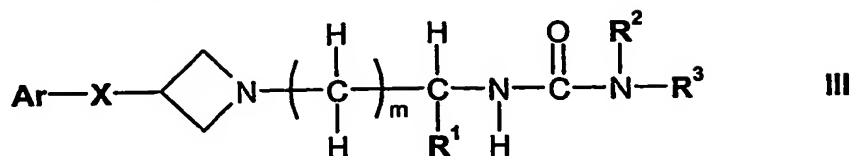
4. A compound according to claim 1, which is of formula II



where

Ar is phenyl substituted by one or two substituents selected from fluorine and chlorine, one of said substituents being para to the indicated group X,
 R¹ is hydrogen, C₁-C₄-alkyl substituted by hydroxy or C₁-C₄-alkoxy, C₁-C₄-alkyl substituted by benzoyloxy or phenoxy-C₁-C₄-alkylcarbonyloxy which are optionally substituted in the benzene ring by at least one substituent selected from C₁-C₄-alkoxy, C₁-C₄-alkylcarbonyl and aminosulfonyl, or C₁-C₄-alkyl substituted by naphthyl,
 R³ is phenyl substituted by one, two or three substituents selected from halogen, cyano, di(C₁-C₄-alkyl)amino, C₁-C₄-alkylcarbonylamino, C₁-C₄-alkoxy, or R³ is naphthyl optionally substituted by fluorine, or R³ is C₁-C₄-alkyl substituted by phenoxy which is optionally substituted by one or two substituents selected from halogen, cyano, C₁-C₄-alkyl, C₁-C₄-alkoxy or C₁-C₄-alkylcarbonyl, or R³ is C₁-C₄-alkyl substituted by benzoyloxy or phenoxy-C₁-C₄-alkylcarbonyloxy which are optionally substituted in the benzene ring by at least one substituent selected from C₁-C₄-alkoxy, C₁-C₄-alkylcarbonyl and aminosulfonyl, or R³ is a heterocyclic group having a 5- or 6-membered heterocyclic ring in which one or two ring atoms are hetero atoms selected from nitrogen, oxygen and sulfur optionally fused to a benzene ring which is optionally substituted by one or two substituents selected from halogen, C₁-C₄-alkoxy and C₁-C₄-alkylcarbonyl,
 X is -O-, and
 m is 2 or 3.

5. A compound according to claim 1, which is of formula III



where

Ar is phenyl substituted by one or two substituents selected from fluorine and chlorine, one of said substituents being para to the indicated group X,

R¹ is hydrogen, C₁-C₄-alkyl substituted by hydroxy or C₁-C₄-alkoxy,

R² is hydrogen or C₁-C₄-alkyl and R³ is C₅-C₉-cycloalkyl, a heterocyclic group having 5 to 11 ring atoms of which one or two are nitrogen or oxygen atoms, phenyl optionally substituted by one, two or three substituents selected from fluorine, chlorine, hydroxy, nitro, C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl or C₁-C₄-alkoxy, phenyl-C₁-C₄-alkyl substituted in the phenyl group by one or two substituents selected from halogen and C₁-C₄-alkyl, C₁-C₄-alkyl substituted by naphthyl, or C₅-C₆-cycloalkyl having a benzo group fused thereto, or R² and R³ together with the nitrogen atom to which they are attached denote a heterocyclic group having a 6-membered N-heterocyclic ring fused to a benzene ring which is optionally substituted by up to 2 C₁-C₄-alkoxy groups,

X is -O- or -C(=O)-, and

m is 2 or 3.

6. A compound according to claim 1, which is also of formula III, where

Ar is phenyl substituted by chlorine para to the indicated group X and optionally also substituted by chlorine meta to the indicated group X,

R¹ is hydrogen or C₁-C₄-alkyl substituted by hydroxy, C₁-C₄-alkoxy or C₁-C₄-acyloxy,

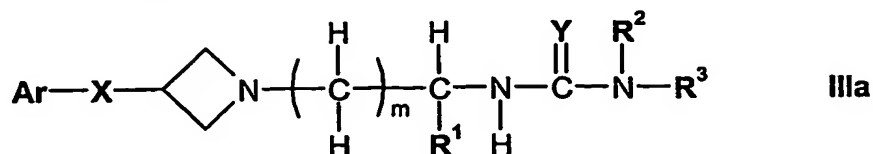
R² is hydrogen,

R³ is a heterocyclic group having 5 to 11 ring atoms of which 1 to 4 are hetero atoms selected from nitrogen, oxygen and sulphur or atoms, or R³ is phenyl optionally substituted by one, two or three substituents selected from halogen, cyano, C₁-C₄-alkyl optionally substituted by C₁-C₄-alkoxy, C₃-C₆-cycloalkyl, C₁-C₄-alkoxy, C₁-C₄-alkoxycarbonyl, (C₁-C₄-alkyl)amino-carbonyl, di(C₁-C₄-alkyl)aminocarbonyl, aminocarbonyl, -SO₂NH₂, -SO₂-C₁-C₄-alkyl and C₁-C₄-acylamino optionally substituted on the nitrogen atom by C₁-C₄-alkyl,

X is -O-, -CH₂- or -C(=O)-, and

m is 2.

7. A compound according to claim 1, which is also of formula IIIa



where

Ar is phenyl optionally substituted by fluoro or chloro para to the indicated group X and/or optionally substituted by fluoro, chloro or C₁-C₄-alkyl meta to the indicated group X;

R¹ is hydrogen or C₁-C₄-alkyl optionally substituted by hydroxy;

R² is hydrogen or C₁-C₄-alkyl;

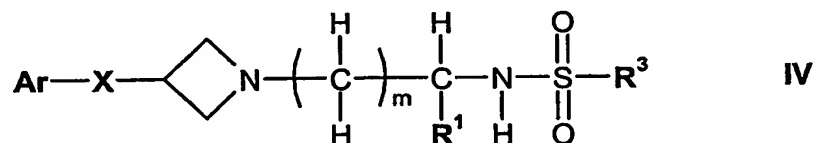
R³ is C₃-C₆-cycloalkyl, or R³ is a heterocyclic group having 5 to 11 ring atoms of which 1 to 4 are hetero atoms selected from nitrogen, oxygen and sulphur or atoms, preferably a heterocyclic ring having 5 atoms of which 1 to 4 are heteroatoms selected from nitrogen, oxygen and sulphur substituted by one or two substituents selected from C₁-C₄-alkyl and C₃-C₆-cycloalkyl, or R³ is phenyl substituted by C₁-C₄-alkoxy;

X is -O-, -CH₂- or -C(=O)-;

Y is O or S; and

m is 1 or 2.

8. A compound according to claim 1, which is of formula IV



where

Ar is phenyl substituted by one or two substituents selected from fluorine and chlorine, one of said substituents being para to the indicated group X,

R¹ is hydrogen or C₁-C₄-alkyl substituted by hydroxy or C₁-C₄-alkoxy,

R³ is phenyl optionally substituted by halogen, C₁-C₄-alkyl or cyano, or R³ is an aromatic N- or S-heterocyclic group having 5 to 10 ring atoms, or R³ is phenyl-C₁-C₄-alkyl,

X is -O- and

m is 2 or 3.

9. A compound according to claim 1, where

Ar is phenyl optionally substituted by one or more substituents selected from halogen, C₁-C₈-alkyl, cyano or nitro,

R¹ is hydrogen or C₁-C₈-alkyl optionally substituted by hydroxy, C₁-C₈-alkoxy, acyloxy, halogen, carboxy, C₁-C₈-alkoxycarbonyl, -N(R⁴)R⁵, -CON(R⁶)R⁷ or by a monovalent cyclic organic group having 3 to 15 atoms in the ring system,

R² is hydrogen or C₁-C₈-alkyl and R³ is C₁-C₈-alkyl substituted by phenyl, phenoxy, acyloxy or naphthyl, or R³ is C₃-C₁₀-cycloalkyl optionally having a benzo group fused thereto, a heterocyclic group having 5 to 11 ring atoms of which 1 to 4 are hetero atoms, phenyl or naphthyl, said phenyl, phenoxy or naphthyl groups being optionally substituted by one or more substituents selected from halogen, cyano, hydroxy, acyl, nitro, -SO₂NH₂, C₁-C₈-alkyl optionally substituted by C₁-C₈-alkoxy, C₁-C₈-haloalkyl, C₁-C₈-alkoxy, C₁-C₈-haloalkoxy, C₁-C₈-alkylthio, -SO₂-C₁-C₈-alkyl, C₁-C₈-alkoxycarbonyl, C₁-C₈-acylamino optionally substituted on the nitrogen atom by C₁-C₈-alkyl, C₁-C₈-alkylamino, aminocarbonyl, C₁-C₈-alkylamino-carbonyl, di(C₁-C₈-alkyl)amino, di(C₁-C₈-alkyl)aminocarbonyl, di(C₁-C₈-alkyl)aminocarbonyl-methoxy, or R² and R³ together with the nitrogen atom to which they are attached denote a heterocyclic group having 5 to 10 ring atoms of which 1, 2 or 3 are hetero atoms,

R⁴ and R⁵ are each independently hydrogen or C₁-C₈-alkyl, or R⁴ is hydrogen and R⁵ is hydroxy-C₁-C₈-alkyl, acyl, -SO₂R⁸ or -CON(R⁶)R⁷, or R⁴ and R⁵ together with the nitrogen atom to which they are attached denote a 5- or 6-membered heterocyclic group,

R⁶ and R⁷ are each independently hydrogen or C₁-C₈-alkyl, or R⁶ and R⁷ together with the nitrogen atom to which they are attached denote a 5- or 6-membered heterocyclic group,

R⁸ is C₁-C₈-alkyl, C₁-C₈-haloalkyl, or phenyl optionally substituted by C₁-C₈-alkyl,

X is -C(=O)-, -O-, -CH₂-, or CH(OH),

Y is oxygen or sulfur,

m is 1, 2, 3 or 4, and

n, p and q are each 0 or 1, n+p+q=1 or 2, n+q=1, p+q=1, and when n is 0, p is 0.

10. A compound according to claim 1, where

Ar is phenyl optionally substituted by one or more substituents selected from halogen, C₁-C₈-alkyl, cyano or nitro,

R¹ is hydrogen or C₁-C₈-alkyl optionally substituted by hydroxy, C₁-C₈-alkoxy, acyloxy, halogen, carboxy, C₁-C₈-alkoxycarbonyl, -N(R⁴)R⁵, -CON(R⁶)R⁷ or by a monovalent cyclic organic group having 3 to 15 atoms in the ring system,

R² is hydrogen or C₁-C₈-alkyl and R³ is C₁-C₈-alkyl substituted by phenyl, phenoxy, acyloxy or

naphthyl, or R³ is C₃-C₁₀-cycloalkyl optionally having a benzo group fused thereto, a heterocyclic group having 5 to 11 ring atoms of which 1 to 4 are hetero atoms, phenyl or naphthyl, said phenyl, phenoxy or naphthyl groups being optionally substituted by one or more substituents selected from halogen, cyano, hydroxy, acyl, nitro, C₁-C₈-alkyl, C₁-C₈-haloalkyl, C₁-C₈-alkoxy, C₁-C₈-haloalkoxy, C₁-C₈-alkylthio, C₁-C₈-alkoxycarbonyl, acylamino, C₁-C₈-alkylamino, di(C₁-C₈-alkyl)amino or di(C₁-C₈-alkyl)aminocarbonylmethoxy, or R² and R³ together with the nitrogen atom to which they are attached denote a heterocyclic group having 5 to 10 ring atoms of which 1, 2 or 3 are hetero atoms,

R⁴ and R⁵ are each independently hydrogen or C₁-C₈-alkyl, or R⁴ is hydrogen and R⁵ is hydroxy-C₁-C₈-alkyl, acyl, -SO₂R⁸ or -CON(R⁶)R⁷, or R⁴ and R⁵ together with the nitrogen atom to which they are attached denote a 5- or 6-membered heterocyclic group,

R⁶ and R⁷ are each independently hydrogen or C₁-C₈-alkyl, or R⁶ and R⁷ together with the nitrogen atom to which they are attached denote a 5- or 6-membered heterocyclic group,

R⁸ is C₁-C₈-alkyl, C₁-C₈-haloalkyl, or phenyl optionally substituted by C₁-C₈-alkyl,

X is -C(=O)-, -O-, -CH₂-, or CH(OH),

Y is oxygen or sulfur,

m is 1, 2, 3 or 4, and

n, p and q are each 0 or 1, n+p+q=1 or 2, n+q=1, p+q=1, and when n is 0, p is 0.

11. A compound according to claim 1 substantially as described in any one of the Examples.

12. A compound according to any one of the preceding claims in combination with another drug substance which is an anti-inflammatory, a bronchodilator or an antihistamine.

13. A compound according to any one of the preceding claims for use as a pharmaceutical.

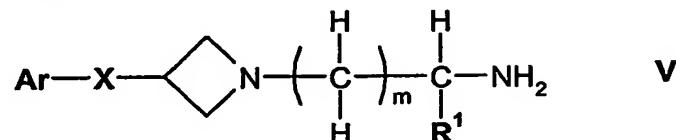
14. A pharmaceutical composition comprising as active ingredient a compound according to any one of claims 1 to 12.

15. The use of a compound according to any one of claims 1 to 12 for the manufacture of a medicament for the treatment of a condition mediated by CCR-3.

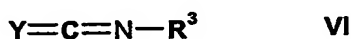
16. Use according to claim 15, in which the condition is an inflammatory or allergic condition, particularly an inflammatory or obstructive airways disease.

17. A process for the preparation of a compound of formula I as claimed in claim 1 which comprises

- (i) (A) for the preparation of compounds of formula I where n is 1, p is 1, q is 0 and R² is hydrogen, reacting a compound of formula V

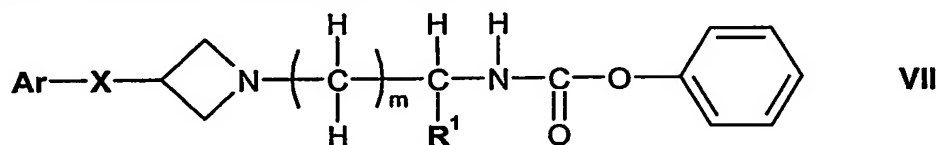


where Ar, X, m and R¹ are as hereinbefore defined, with a compound of formula VI

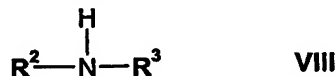


where Y and R³ are as hereinbefore defined, with the proviso that when R¹ contains a reactive functional group it may be in protected form, and, where R¹ in the product contains a protected functional group, replacing the protecting group by hydrogen;

- (B) for the preparation of compounds of formula I where n is 1, p is 1, q is 0 and R² is hydrogen or C₁-C₈-alkyl, reacting a compound of formula VII



where Ar, X, m and R¹ are as hereinbefore defined, with a compound of formula VIII

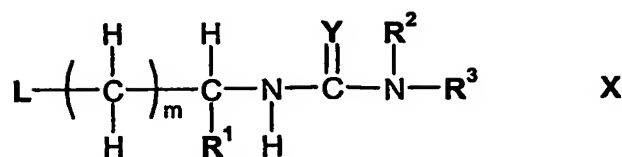


where R² and R³ are as hereinbefore defined, or and, where R¹ in the product contains a protected functional group, replacing the protecting group by hydrogen;

- (C) for the preparation of compounds of formula I where n is 1, p is 1, q is 0 and R² and R³ together with the nitrogen atom to which they are attached denote a heterocyclic group, reacting a compound of formula IX

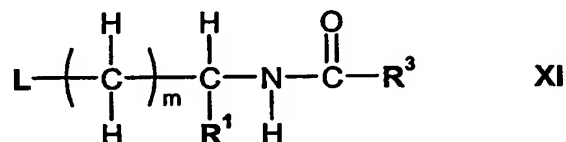


where Ar and X are as hereinbefore defined, with a compound of formula X



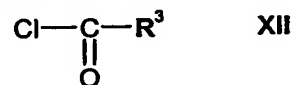
where m, R¹ and Y are as hereinbefore defined, R² and R³ together with the nitrogen atom to which they are attached denote a heterocyclic group having 5 to 10 ring atoms of which one, two or three are hetero atoms, and L is halogen, preferably bromine;

(D) for the preparation of compounds of formula I when n is 1, p is 0, q is 0 and Y is oxygen, reacting a compound of formula IX where Ar and X are as hereinbefore defined, with a compound of formula XI



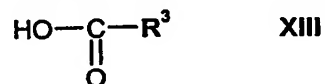
where L, m, R¹ and R³ are as hereinbefore defined;

(E) for the preparation of compounds of formula I where n is 1, p is 0, q is 0 and Y is oxygen, reacting a compound of formula V where Ar, X, m and R¹ are as hereinbefore defined, with a compound of formula XII



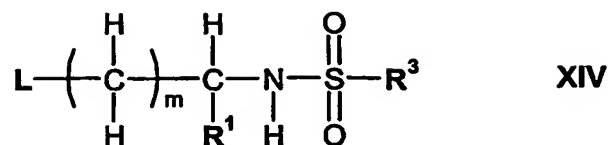
where R³ is as hereinbefore defined, and, where R¹ in the product contains a protected functional group, replacing the protecting group by hydrogen;

(F) for the preparation of compounds of formula I where n is 1, p is 0, q is 0, R² is hydrogen and Y is oxygen, reacting a compound of formula V where Ar, X, m and R¹ are as hereinbefore defined, with a compound of formula XIII



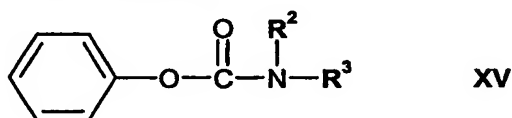
where R³ is as hereinbefore defined, and, where R¹ in the product contains a protected functional group, replacing the protecting group by hydrogen;

(G) for the preparation of compounds of formula I where n is 0, p is 0, and q is 1, reacting a compound of formula IX where Ar and X are as hereinbefore defined in the form of a hydrohalide salt with a compound of formula XIV



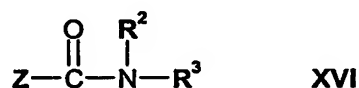
where L, m, R¹ and R³ are as hereinbefore defined;

(H) for the preparation of compounds of formula I where n is 1, p is 1, q is 0 and Y is oxygen, reacting a compound of formula V where Ar, X, m and R¹ are as hereinbefore defined, with a compound of formula XV



where R² and R³ are as hereinbefore defined; or

(I) for the preparation of compounds of formula I where n is 1, p is 0, q is 0, Y is oxygen and R² is C₁-C₈-alkyl or C₃-C₁₀-cycloalkyl, reacting a compound of formula V where Ar, X, m and R¹ are as hereinbefore defined, with a compound of formula XVI



where R² is C₁-C₈-alkyl or C₃-C₁₀-cycloalkyl, R³ is as hereinbefore defined and Z is a halogen, with the proviso that when R¹ contains a reactive functional group it may be in protected form, and, where R¹ in the product contains a protected functional group, replacing the protecting group by hydrogen; and

- (ii) recovering the product in free or salt form.